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ORIGINAL ARTICLE

^1H proton MR spectroscopy and diffusion-weighted imaging in discrimination between pyogenic brain abscesses and necrotic brain tumors



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KEYWORDS

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Abstract *Background:* Differentiation between cerebral abscesses and necrotic brain tumors showing ring enhancement can be confusing at times by conventional MRI. The introduction of advanced imaging techniques, such as MR spectroscopy and diffusion WI, have contributed to the differentiation.

The purpose of this study is to test the hypothesis that MR spectroscopy and diffusion weighted can be used to differentiate between necrotizing or cystic brain tumor and brain abscesses.

Methods: The study was conducted on 45 patients (necrotic or cystic tumor (30 cases); brain abscess (15 cases) showing ring-shaped contrast enhancement on conventional MRI. 1.5-T ^1H -MR Spectroscopy and diffusion WI were performed and the results were ensured by stereotactic biopsy or aspiration procedures in surgically indicated cases and/or follow up.

Results: 14 patients (out of 15) with pyogenic abscess had lactate, amino acids, and acetate peaks; Succinate peak is seen as extra peak in three of these patients, and lipid peaks are also seen as extra peaks in 3 patients. One patient with brain stem abscess after 20 days treatment by antibiotics shows only lactate and lipid peaks. 2 of them show mild increase in choline with decrease in NAA (brain tissue contamination).

Abbreviations: AAs, amino acids; Ac, acetate; DWI, diffusion-weighted imaging; ^1H -MR spectroscopy, hydrogen 1 proton magnetic resonance spectroscopy; NAA, N-acetyl aspartate; Ch, choline; Cr, creatine; Lac, lactate; Lip, lipid; SE, spin-echo; Suc, succinate; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; ADC, apparent diffusion coefficient; MRI, magnetic resonance imaging; 1.5 T, 1.5 tesla; TE, echo time; ROI, region of interest; PPV, positive predictive value; NPV, negative predictive value

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17 out of 30 patients with cystic or necrotic tumor showed only lactate peak in MRS. While 13 patients show lactate and lipid peaks, four of them show additional high choline peak with low NAA and creatine peak (contamination with brain tissue).

The results were confirmed by Stereotactic biopsy in 27 cases and aspiration in 13 cases and follow up for all cases.

The sensitivity, specificity, PPV, NPV and overall accuracy of diffusion and MRS were 88%, 100%, 100%, 93.3% and 95.5% respectively.

Conclusion: ^1H -MRS and diffusion WI are fast, easy to perform, noninvasive, and provide additional information that can accurately differentiate between necrotic/cystic tumors and cerebral abscesses.

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1. Introduction

Attempts to differentiate brain abscesses from cystic or necrotic brain tumors at computed tomography (CT) or magnetic resonance (MR) imaging have met with little success, although the diagnosis can, in some cases, be suggested at a detailed analysis of the capsule, as brain abscess surrounded by hypointense capsule especially in T2 WI in the capsule-formation stage. Difficulties in the diagnosis of intracranial abscess are mainly due to the combination of often unspecified clinical findings and similarities in the morphologic appearance of some intracranial mass lesions, such as cystic gliomas, metastases, and brain abscesses (1,2).

Diffusion-weighted imaging provides a useful tool to evaluate the diffusion properties of water molecules in tissue. A marked difference in the signal intensity on diffusion-weighted imaging between brain abscesses and necrotic or cystic tumors may be due to different physical and biochemical components of the central contents. Pus in an abscess cavity is a thick, mucoid, acidic greenish yellow fluid that consists of inflammatory cells, bacteria, necrotic tissue, and proteinaceous exudate with high viscosity. In highly viscous fluid, the velocity of gross movement of fluid is markedly decreased and so is the microscopic diffusional motion of water molecules (2).

In contrast, the cystic or necrotic cavities of brain tumors usually consist of necrotic tumor tissue debris, fewer inflammatory cells than in an abscess and more clear serous fluid than pus (2,3). So the abscess shows restricted diffusion in diffusion WI, with low ADC value, while the tumor cavity shows free diffusion with high ADC value (2). Markedly increased signal intensity of a rim-enhancing brain mass on diffusion-weighted imaging and a low ADC indicating restricted water diffusion are features that should suggest the diagnosis of brain abscess, but are not specific for this diagnosis (4,5).

In vivo ^1H MR spectra from brain abscesses show the assignment of various resonances of acetate (*Ac*), alanine (*Ala*), lactate (*Lac*), and amino acids (*AA*). At a TE of 144, the phase reversal resonances are well depicted at 1.5, 1.3, and 0.9 ppm, which confirms the assignment to alanine, lactate, and amino acids respectively (6,7). MRS of necrotizing brain tumors, voxels in the center necrotizing part shows mainly increase lactate peak especially at short TE sequence that may be inverted at a TE of 144 (8–12).

Treatment of a brain abscess involves aspiration of the pus or excision of the abscess, followed by parenteral prolonged antibiotic therapy (usually 4–8 weeks). Emergent surgery

should be performed if a single abscess is present. Abscesses larger than 2.5 cm are excised or aspirated, while those smaller than 2.5 cm or which are at the cerebritis stage are aspirated for diagnostic purposes only. In cases of multiple abscesses or in abscesses in essential brain areas, repeated aspirations are preferred to complete excision. High-dose antibiotics for an extended period may be an alternative approach in this group of patients (13–15).

The purpose of this study is to determine the sensitivity of in vivo hydrogen magnetic resonance (MR) spectroscopy and diffusion weighted imaging to differentiate between brain abscesses and necrotizing or cystic brain tumors.

2. Methods

Approval of Research Ethics Committee (REC) and informed written consent were obtained from all participants in the study.

A prospective study carried out between July 2010 to June 2012, 1.5 tesla ^1H -MRS and diffusion-weighted imaging were performed in 45 consecutive patients (28 male and 17 female; age range, 16–74 years with mean 45.3 years) with necrotic lesions and MR imaging evidence of ring-shaped enhancement after the injection of contrast material were referred to radio-diagnosis department.

Stereotactic biopsy and/or aspiration procedures were/was done at the Neurosurgical department. Cosman–Roberts–Wells (CRW), stereotactic frame supported by multiplanar reconstruction software, (Prazis plus 3) was used under computerized tomography (CT) or magnetic resonance imaging (MRI) guidance to ensure proper tissue sampling from the lesions.

2.1. MR imaging and proton MR spectroscopy

All patients were examined using a 1.5-T MRI system (Signa; GE Medical Systems,) with a quadrature head coil.

Sedation was needed for 10 patients (for convulsion and abnormal movements).

Inclusion criteria for this study were presence of necrotic marginally enhanced lesion in the brain on conventional MRI. 3 patients were excluded due to associated hemorrhagic changes (1 case) and close proximity from skull bone (2 cases).

All patients were examined in the supine position using standard quadrature head coil with the head maintained in a

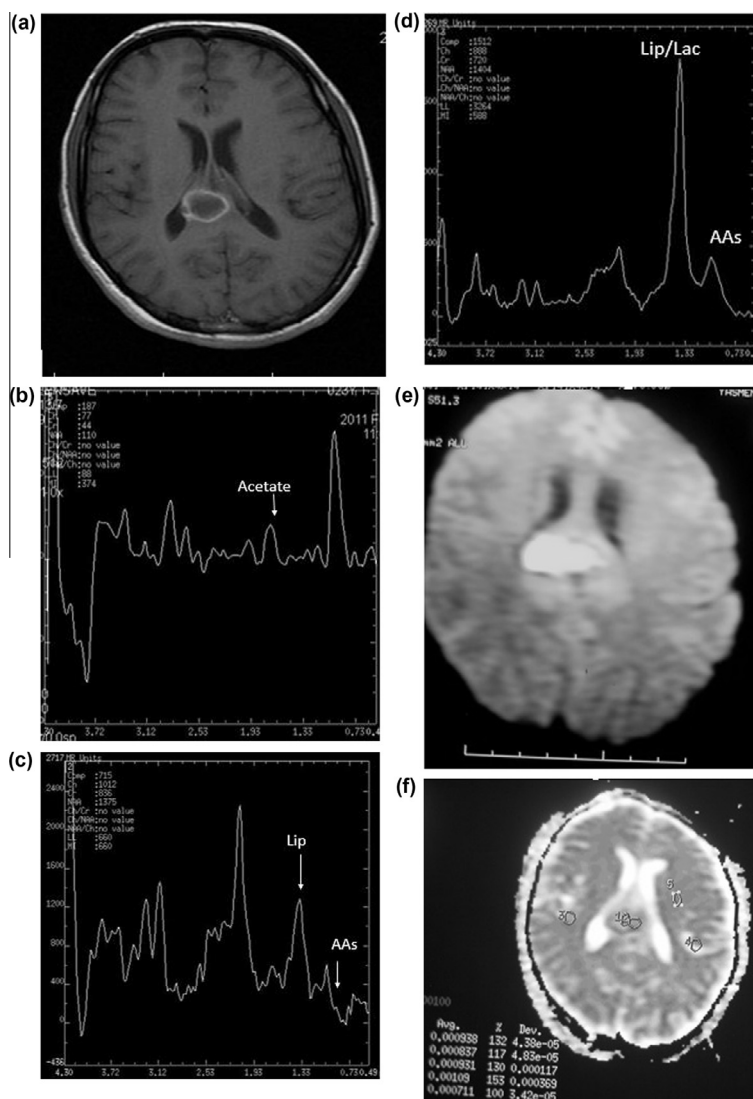


Fig. 1 Pyogenic brain abscess. Female patient aged 23 years complaining from headache, fever and blurred vision. Axial T1 with contrast shows marginally enhanced lesion in the splenium of corpus callosum (Fig. 1a). MRS at the lesion core shows elevated acetate (Ac), lipids, lactate (Lac) and amino acids peaks (Fig. 1b–d). Diffusion WI shows restricted diffusion of the lesion core, mean ADC value $0.7 \times 10^{-3} \text{ mm}^2/\text{s}$ (Fig. 1e and f). (a) Axial T1 with contrast, (b and c) MR Spectroscopy (TE 144), (d) MR spectroscopy (TE35), (e) Diffusion weighted image, (f) ADC map.

neutral position. The routine imaging studies included MRI. Routine spin echo (SE) T2 (TR/TE = 2200/20, 80) and T1 weighted (TR/TE = 660/15) images were obtained in the axial coronal and sagittal planes, contrast material (Gd DPTA) (Magnevist) injected IV with a dose of 0.1 mmol/kg.

We used axial T1 with contrast weighted imaging to locate the multivoxels for the ^1H -MRS studies. We select the voxel in the estimated center of the lesion (however in 6 patients the size of the voxel is larger than the center of the lesion revealing contamination by brain tissue), another voxels are located in the wall of the lesions, perilesional, surrounding edema and in the contralateral apparently normal side.

Optimal water resonance suppression was achieved. Measurement parameters were 1700/180/2 (TR/TE/excitations), 16×16 phase-encoding steps, $160 \times 160 \text{ mm}$ field of view, 14 mm section thickness and 1024 data points, a spectral width of 2500 Hz, for all patients. In all patients, MR spectra were

obtained with a TE of 144 with additional TE 270 and/or 35. The acquisition time for each sequence was 7 min 54 s.

2.2. Diffusion-weighted imaging and apparent diffusion coefficient mapping

Diffusion-weighted imaging was performed in the transverse plane by using an SE echo-planar imaging sequence with the following parameters: TR/TE/TI (inversion time), 12,000/95/2200 ms; diffusion gradient encoding in three orthogonal directions; $b = 1000 \text{ s/mm}^2$; FOV, $24 \times 24 \text{ cm}$; matrix size, 128×256 pixels; section thickness, 5 mm; section gap, 1 mm. An ADC map was obtained. In quantitative study, an imaging slice was chosen, five (1- to 2-cm) circular region of interest were located on the center of the lesion mainly (confined within the abscess cavity and the necrotic or cystic portion of the brain tumor), as well as the peripheral portion and normal

appearing white matter, mean ADC value is calculated for each.

The diagnosis was done by gathering findings of MRI, proton MR spectroscopy (^1H -MRS) and diffusion-weighted imaging.

Sterotactic biopsy is done for 27 cases and aspiration for 13 cases and follow up for all cases.

2.3. Statistical analysis

Statistical presentation and analysis of the present study were conducted, using the mean and standard deviation by SPSS V.16. Analysis of variance [ANOVA] tests and Tukey's test were used to determine the significance between 2 groups: According to the computer program SPSS for Windows. ANOVA test was used for comparison among different times in the same group in quantitative data. P value < 0.05 was considered significant.

3. Results

45 patients presented with necrotic or cystic tumor (30 cases) and brain abscess (15 cases) showing ring-shaped enhanced lesions after contrast agent administration on conventional MRI.

The tumors were glioblastomas (19 patients), pilocytic astrocytoma (8 patients) and metastases (3 patients) with primary malignancy, bronchogenic carcinoma in two cases and hepatoma in one case. The tumors were located in the temporo-parietal lobe ($n = 13$), occipital ($n = 9$), frontal ($n = 4$), suprasellar (1), pons (1) and multifocal ($n = 2$). The abscesses were located in the frontal (4), the parietal (5), Splenium of corpus callosum ($n = 1$), midbrain ($n = 1$) and multifocal ($n = 4$).

The main resonances in ^1H -MRS of brain abscess were the resonances of amino acids (valine, leucine, and isoleucine) (0.9 ppm), acetate (1.9 ppm), and lactate (1.3 ppm) identified

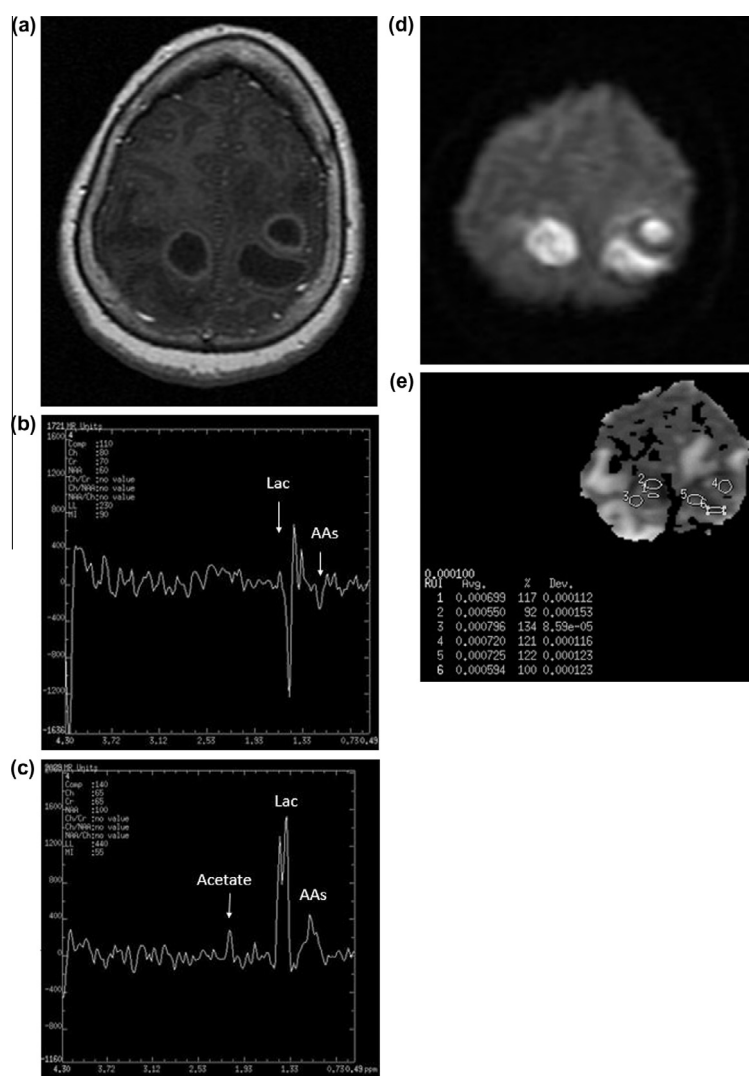


Fig. 2 multiple pyogenic brain abscesses. Female patient aged 55 years complaining from dizziness, fever and seizures. Axial T1 with contrast shows multifocal marginally enhanced cerebral lesions (Fig. 2a). MRS at the lesion core shows high acetate (Ac) lactate (Lac), and amino acids (AA) peaks with evidence of J coupling at 0.9 and 1.3 denoting presence of amino acids and lactate. (Fig. 2b and c). Diffusion WI shows restricted diffusion of the lesion core, mean ADC value $0.5 \times 10^{-3} \text{ mm}^2/\text{s}$ (Fig. 2d and e). (a) Axial T1 with contrast, (b) MR Spectroscopy (TE 144), (c) MR spectroscopy (TE35), (d) diffusion weighted image, (e) ADC map.

Table 1 ¹H-MRS imaging findings in 45 patients with brain abscess (*n* = 10) and necrotic tumors (*n* = 15).

Metabolite detected	Site of metabolite (ppm)	No. of cases of abscess (15)	No. of cases of tumors (30)
Lactate	1.3	15	30
Lipid	0.9–1.3	4	13
Acetate	1.9	14	0
Succinate	2.4	3	0
Amino acids	0.9	14	0
Choline	3.2	2 (++)	4 (++++)
NAA	1.9	2 (++)	4 (+)
Creatine	3	2 (++)	4 (+)

The mark (+) are arbitrarily assigned to one of three grades, low (+), medium (++), or high (+++), relative to the peak height of water.

in 14 patients (Fig. 2). An extra succinate peak (2.4 ppm) was also detected in 3 of these patients, and lipids peak (0.9-1.3 ppm) are seen also as extra peaks in 3 patients (Fig. 1). One patient with treated abscess in midbrain shows only lactate and lipid peaks. 2 of them show a mild increase in choline with decrease in NAA (brain tissue contamination with relatively small size of the lesions). Differentiation between lipids detected at 0.8–1.2 ppm and amino acids detected at 0.9 ppm by evidence of J coupling at TE 144 of amino acids (Table 1).

Spectra of 17 patients with cystic or necrotic tumor showed only the peak attributed to lactate. Lactate and lipid were found in 13 patients, four of them show additional high choline peak with low NAA and Creatine peak (contamination with brain tissue) (Fig. 3) (Table 1).

On diffusion study, the central portion of brain abscesses (15 patients) show restricted diffusion in diffusion WI

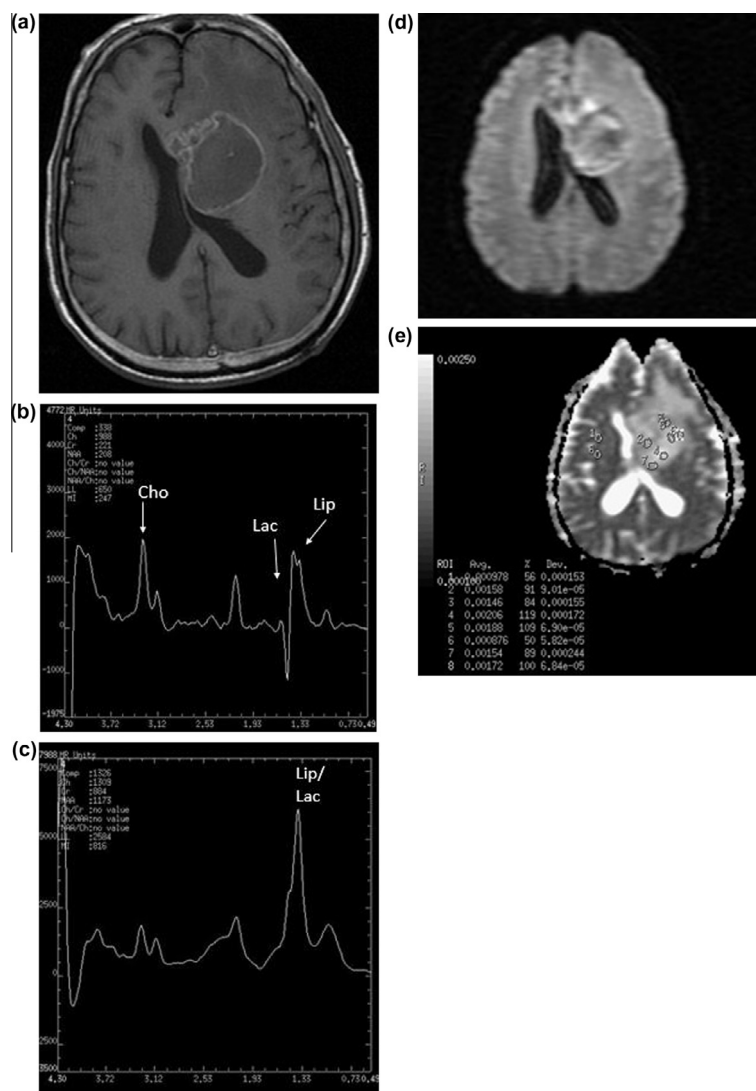


Fig. 3 Glioblastoma multiforme grade IV. Male patient aged 63 years complaining from headache, hemiparesis and dizziness. Axial T1 with contrast shows irregular marginally enhanced complex lesion in the left temporo-parietal lobes (Fig. 3a). MRS from the lesion core shows a high lactate (Lac) and lipid peaks (Fig. 3b and c). Diffusion-weighted image shows free diffusion of necrotic part of tumor, mean ADC value is $1.6 \times 10^{-3} \text{ mm}^2/\text{s}$ (Fig. 3d and e). (a) Axial T1 with contrast, (b) MR Spectroscopy (TE 144), (c) MR spectroscopy (TE35), (d) Diffusion weighted image, (e) ADC map.

Table 2 Diffusion WI and ADC values findings in the abscess and tumor cases.

Cases		Diffusion WI	Mean ADC value $\times 10^{-3} \text{ mm}^2/\text{s}$
Abscess	Central region	Restricted (15 cases)	0.54 ± 0.19
	Peripheral region	Free (15 cases)	1.76 ± 0.15
Tumors	Central region	Free (28 cases)	1.91 ± 0.08
		Mild restricted (2 cases)	
	Peripheral region	Restricted	0.36 ± 0.32

Table 3 The sensitivity, specificity, positive and negative predictive values and over all accuracy of MRS and diffusion WI in differentiation between brain abscesses and necrotic/cystic brain tumors.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Diffusion and MRS	88	100	100	93.3	95.5

(markedly hyperintense) (Figs. 1 and 2), whereas the necrotic or cystic content of the brain tumors (28 patients) show free diffusion (hypointense) (Fig. 3) while 2 cases reveal mild restricted diffusion as a result of contamination from previous biopsy. On quantitative assessment, the mean ADC value of the abscess cavity was $0.54 \pm 0.19 \times 10^{-3} \text{ mm}^2/\text{s}$ while $1.91 \pm 0.08 \times 10^{-3} \text{ mm}^2/\text{s}$ for the necrotic part of the tumor (Table 2). (The difference between the mean ADC values of abscess and necrotic tumors was statistically significant ($P < 0.001$). No statistically significant differences were found in ADC values among the different abscesses or among the different necrotic tumors).

The combination of ^1H -MRS and diffusion-weighted imaging increases the diagnostic accuracy of differentiation between brain abscesses and cystic or necrotic brain tumors. The 15 cases of abscess perfectly match with stereotactic biopsy, while out of 30 cases of tumors 2 are diagnosed by spectroscopy and diffusion WI as low grade tumours and by surgical biopsy and histopathologically as grade IV glioblastoma multiform and two cases as abscess and as necrotic tumor by biopsy and this due to infected tumoral necrotic material biopsy.

Sensitivity, specificity, PPV, NPV and overall accuracy of MRS and diffusion WI (Table 3).

4. Discussion

In this study, we focused on the ability of ^1H MR spectroscopy and diffusion weighted imaging to resolve the clinical and radiological problems in discriminating brain abscesses from cystic or necrotic tumors.

With recent development of modalities and imaging techniques, it is important to evaluate the accuracy and assess the variations of imaging findings that support clinical diagnosis.

We discuss imaging findings of DWI and MR spectroscopy in patients with moderate number of brain abscess and necrotic/cystic tumors proven by stereotactic biopsy or aspiration which testified the result of previous studies.

45 patients were collected from wards and clinics of neurosurgery departments, with MR imaging evidence of ring-shaped enhancement after the injection of contrast material.

The neuroimaging appearance of some cystic or necrotic tumors is similar to that of brain abscesses and the medical management strategies for abscess and neoplasm are different (1).

The spectral characteristics of intracranial abscesses can be summarized as follows: absence of NAA (detected at 2.0 ppm), absence of choline (detected at 3.2 ppm); absence of Cr (detected at 3.0 ppm), presence of cytosolic amino acids such as leucine, isoleucine, and valine (detected at 0.9 ppm); presence of lactate (detected at 1.3 ppm), acetate (detected at 1.92 ppm), succinate (detected at 2.4 ppm), and alanine (detected at 1.5 ppm); and occasionally lipids (mostly short-chain fatty acids such as butyric, isobutyric, caproic, propionic, valeric, and isovaleric acids, detected at 0.8–1.2 ppm (1,16).

In the study of Lai et al. (1) who studied on fourteen patients (necrotic or cystic tumor [$n = 7$]; pyogenic abscess [$n = 7$]) underwent 1.5-T ^1H -MRS and diffusion-weighted imaging and had findings of ring-shaped enhancement after contrast agent administration, stated that all cystic tumors and abscesses in their study showed findings of increased lactate, which is a nonspecific metabolite that results from anaerobic glycolysis. And this agrees with our study as all 45 cases (necrotic tumors [$n = 30$], pyogenic abscess [$n = 15$]) show lactate peak.

Lai et al. (17) reported a decline of the acetate and pyruvate in five patients after 1 week of aspiration and medical treatment. They think that the disappearance of metabolites of bacterial origin suggests a positive response to therapy.

Kapsalakia and Fountasa, (18) who study the application of proton MR (^1H -MR) spectroscopy in the imaging evaluation of patients harboring intracranial abscess, they concluded that the detection of cytosolic amino acids is a strong indication of an abscess of pyogenic origin and ^1H -MR spectroscopy constitutes a valuable diagnostic tool for intracranial abscesses, and this agrees with the present study as amino acids were detected in 14 cases out of 15, one case of treated abscess shows good response to therapy as all resonances (representing succinate, acetate, alanine, and amino acids), except that of lactate, had disappeared and so we agree with previous studies that conclude that ^1H -MR spectroscopy constitutes a valuable diagnostic tool for intracranial abscesses, evaluating their evolution and treatment response (18–20).

Diffusion-weighted imaging is an easy and fast sequence in distinguishing between brain abscesses and cystic or necrotic brain tumors. Server et al. (21) reported that Brain abscess displays high signal intensity on diffusion-weighted images with low ADC value. The pus consistency itself could account for

the restricted diffusion and therefore high diffusion-weighted imaging signal intensity. Subsequent studies showed the same results (4,8,22). All cases of pyogenic brain abscesses showed restricted diffusion and were in good agreement with the findings of these previous studies.

Ohba et al. (4) concluded that markedly increased signal intensity of a rim-enhancing brain mass on diffusion-weighted imaging and a low ADC indicating restricted water diffusion are features that should suggest the diagnosis of brain abscess, but are not specific for this diagnosis, this does not agree with our results as all cases of brain abscesses showed restricted diffusion and this is mostly due to relatively low number of cases in our study (15 cases).

We coincide with the previous studies (4,23) that the mean ADC ratios for all pyogenic abscesses were $0.54 \pm 0.19 \times 10^{-3} \text{ mm}^2/\text{s}$ and this variation might be related to a difference in the concentration of inflammatory cells, and immune response of patients.

Our results indicate that the amino acids are detectable in 14 cases of abscesses and not seen in cases of necrotic tumor, which is not in agreement with the results of Bartusik et al. (24) that document the visibility of amino acids in the 0.9-ppm region with a 136-ms TE in cases of brain tumors.

Nath et al. (2) reported two cases of cystic or necrotic brain metastasis with markedly high signal intensity on diffusion-weighted images. Surgery revealed that the cyst had a thick and creamy necrotic content similar to pus.

In the study of Chiang et al. (25) as the aim of their study is distinction between pyogenic brain abscess and necrotic brain tumor using 3-tesla MR spectroscopy, diffusion and perfusion imaging resulted that on diffusion-weighted MR images, the central cavities of the cerebral abscesses had very low ADCs, which accounted for the signal hypointensity on ADC map images and the mean ADC values at the central cavities of the cerebral abscesses to be significantly lower than in necrotic tumors, and this coincides with our results of restricted diffusion and lower ADC values in all cases of abscesses cavity versus necrotic/cystic brain tumors (25).

¹H-MRS is limited in cases of smaller peripheral lesions, skull base lesions, hemorrhagic lesions cause inhomogeneity in the voxel and contaminate the spectra. The small number of abscess cases decreases the statistical strength.

5. Conclusions

¹H-MRS and diffusion-weighted imaging are fast, easy to perform, noninvasive, and provide additional information that can accurately differentiate between necrotic/cystic tumors and pyogenic cerebral abscesses. ¹H MR resonances from succinate (2.4 ppm), acetate (1.9 ppm), and from amino acids (valine, leucine, and isoleucine (0.9 ppm region) are diagnostic abscess markers.

The use of MR spectroscopy in combination with DW imaging can significantly increase the diagnostic accuracy of conventional MR imaging and provide valuable preoperative information regarding the nature of ring-enhancing intracranial lesions.

Conflict of interest

None.

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